swissmedic

*Date:* 9 April 2025
Swissmedic, Swiss Agency for Therapeutic Products

# *Swiss Public Assessment Report*
## *Extension of therapeutic indication*

# Nilemdo

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| **International non-proprietary name:** | bempedoic acid |
| **Pharmaceutical form:** | Film-coated tablet |
| **Dosage strength(s):** | 180 mg |
| **Route(s) of administration:** | oral |
| **Marketing authorisation holder:** | Daiichi Sankyo (Schweiz) AG |
| **Marketing authorisation no.:** | 67583 |
| **Decision and decision date:** | extension of therapeutic indication approved on 31 January 2025 |

**Note:**

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

**Table of contents**

# 1 Terms, Definitions, Abbreviations

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|---|---|
| ADA | Anti-drug antibody |
| ADME | Absorption, distribution, metabolism, elimination |
| AE | Adverse event |
| ALT | Alanine aminotransferase |
| API | Active pharmaceutical ingredient |
| ASCVD | Atherosclerotic cardiovascular disease |
| AST | Aspartate aminotransferase |
| ATC | Anatomical Therapeutic Chemical classification system |
| AUC | Area under the plasma concentration-time curve |
| $AUC_{0\text{-}24h}$ | Area under the plasma concentration-time curve for the 24-hour dosing interval |
| CI | Confidence interval |
| $C_{max}$ | Maximum observed plasma/serum concentration of drug |
| CVD | Cardiovascular disease |
| CYP | Cytochrome P450 |
| DDI | Drug-drug interaction |
| EMA | European Medicines Agency |
| ERA | Environmental risk assessment |
| FDA | Food and Drug Administration (USA) |
| GI | Gastrointestinal |
| GLP | Good Laboratory Practice |
| HeFH | Heterozygous familial hypercholesterolaemia |
| HPLC | High-performance liquid chromatography |
| $IC/EC_{50}$ | Half-maximal inhibitory/effective concentration |
| ICH | International Council for Harmonisation |
| Ig | Immunoglobulin |
| INN | International non-proprietary name |
| ITT | Intention-to-treat |
| LDL-C | Low-density lipoprotein cholesterol |
| LoQ | List of Questions |
| MAH | Marketing authorisation holder |
| Max | Maximum |
| Min | Minimum |
| MRHD | Maximum recommended human dose |
| N/A | Not applicable |
| NO(A)EL | No observed (adverse) effect level |
| PBPK | Physiology-based pharmacokinetics |
| PD | Pharmacodynamics |
| PIP | Paediatric investigation plan (EMA) |
| PK | Pharmacokinetics |
| PopPK | Population pharmacokinetics |
| PSP | Pediatric study plan (US FDA) |
| RMP | Risk management plan |
| SAE | Serious adverse event |
| SwissPAR | Swiss Public Assessment Report |
| TEAE | Treatment-emergent adverse event |
| TPA | Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21) |
| TPO | Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21) |
| WHO | World Health Organisation |

# 2 Background information on the procedure

## 2.1 Applicant's request(s)

**Extension(s) of the therapeutic indication(s)**
The applicant requested the addition of a new therapeutic indication or modification of an approved one in accordance with Article 23 TPO.

## 2.2 Indication and dosage

### 2.2.1 Requested indication

Nilemdo is indicated as an adjunct to diet in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- **alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.**

**Nilemdo is indicated in addition to the correction of other risk factors in adults with known, or at high risk for, atherosclerotic cardiovascular disease to reduce cardiovascular risk by lowering LDL-C-levels:**

- in combination with the maximum tolerated dose of a statin with or without other lipid-lowering therapies or,
- **alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.**

### 2.2.2 Approved indication

*Hypercholesterolaemia and mixed dyslipidaemia*
Nilemdo is indicated as an adjunct to diet in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia:

- in combination with a statin or statin with other lipid lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- **as monotherapy or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.**

*Cardiovascular disease*
**Nilemdo is indicated in adults with established, or at high risk for, atherosclerotic cardiovascular disease to reduce cardiovascular risk by lowering LDL-C levels and as an adjunct to correction of other risk factors:**

- in patients on a maximum tolerated dose of a statin with or without ezetimibe or,
- **as monotherapy or in combination with ezetimibe in patients who are statin-intolerant, or for whom a statin is contraindicated.**

**See "Pharmacological Properties" for study results with respect to effects on LDL-C, cardiovascular events and populations studied.**

### 2.2.3 Requested dosage

No change to the dosage recommendation was requested with the application for extension of indication.

### 2.2.4 Approved dosage

(see appendix)

## 2.3 Regulatory history (milestones)

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|---|---|
| Application | 01 January 2024 |
| Formal objection | 08 January 2024 |
| Response to formal objection | 24 March 2024 |
| Formal control completed | 28 March 2024 |
| List of Questions (LoQ) | 13 August 2024 |
| Response to LoQ | 11 September 2024 |
| Preliminary decision | 12 November 2024 |
| Response to preliminary decision | 15 December 2024 |
| Final decision | 31 January 2025 |
| Decision | approval |

# 3 Medical context

Hyperlipidaemia is a diverse group of disorders characterised by an excess of different lipid entities (i.e. triglycerides, cholesterol and phospholipids) in the blood. Hypercholesterolaemia refers to elevated levels of cholesterol in the bloodstream, while primary hypercholesterolaemia is any hypercholesterolaemia caused by a familial or nonfamilial disorder in lipid metabolism. One such disorder is heterozygous familial hypercholesterolaemia (HeFH), which affects between 1:200 and 1:500 individuals globally. In this population, lowering cholesterol has been proven to reduce the risk of cardiovascular disease (CVD).

# 4 Nonclinical aspects

The applicant did not submit any new nonclinical studies to support the requested extension of the indication, which is considered acceptable. From the nonclinical point of view, there are no objections to the approval of the requested extension of the indication.

# 5 Clinical aspects

The evaluation of the clinical data of this application has been carried out in reliance on previous regulatory decisions by EMA. The available assessment report (EMEA/H/C/004958/II/0031) and respective product information were used as a basis for the clinical evaluation.
For further details concerning clinical pharmacology, dosing recommendations, efficacy and safety, see Chapter 7 of this report.

# 6 Risk management plan summary

The RMP summaries contain information on the medicinal products' safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

# 7 Appendix

## Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Nilemdo, film-coated tablets was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

**Note:**
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

# Nilemdo 180 mg film-coated tablets

## Composition

*Active substances*

Bempedoic acid

*Excipients*

Tablet core:
Lactose monohydrate 30 mg; cellulose, microcrystalline; sodium starch glycolate (type A); hydroxypropyl cellulose; magnesium stearate; silica, colloidal anhydrous.
Film-coating:
Poly(vinyl alcohol), talc, titanium dioxide, macrogol.
1 film-coated tablet contains 0.97 mg of sodium.

## Pharmaceutical form and active substance quantity per unit

Each film-coated tablet contains 180 mg of bempedoic acid.
White to off-white, oval, film-coated tablet debossed with “180” on one side and “ESP” on the other side.

## Indications/Uses

*Hypercholesterolaemia and mixed dyslipidaemia*

Nilemdo is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- as monotherapy or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

*Cardiovascular disease*

Nilemdo is indicated in adults with established or at high risk for atherosclerotic cardiovascular disease to reduce cardiovascular risk by lowering LDL-C levels, as an adjunct to correction of other risk factors:

- in patients on a maximum tolerated dose of a statin with or without ezetimibe or,
- as monotherapy or in combination with ezetimibe in patients who are statin-intolerant, or for whom a statin is contraindicated.

For study results with respect to effects on LDL-C, cardiovascular events and populations studied see section "Properties/Effects".

**Dosage/Administration**

Posology

*Usual dosage*

The recommended dose of Nilemdo is one film-coated tablet of 180 mg taken once daily.

*Dose adjustment in the event of concomitant treatments*

For dosage recommendations in the event of concomitant treatments, see section “Interactions”.

*Concomitant simvastatin therapy*

When Nilemdo is coadministered with simvastatin, simvastatin dose should be limited to 20 mg daily (or 40 mg daily for patients who can tolerate simvastatin 80 mg daily longterm without any signs of muscle toxicity) (see sections “Warnings and precautions” and “Interactions”).

*Special populations*

*Patients with hepatic impairment*

No dose adjustment is necessary in patients with mild or moderate hepatic impairment (Child-Pugh A or B). No data are available in patients with severe hepatic impairment (Child-Pugh C). Periodic liver function tests should be considered for patients with severe hepatic disorder (see sections “Warnings and precautions” and “Pharmacokinetics”).

*Patients with renal impairment*

No dose adjustment is necessary in patients with mild or moderate renal impairment. There are limited data available in patients with severe renal impairment (defined as estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 $m^2$), and patients with end-stage renal disease (ESRD) on dialysis have not been studied. Additional monitoring for adverse reactions may be warranted in these patients when Nilemdo is administered (see sections “Warnings and precautions” and “Pharmacokinetics”).

*Elderly patients*

No dose adjustment is necessary in elderly patients (see section “Pharmacokinetics”).

*Children and adolescents*

The safety and efficacy of Nilemdo in children and adolescents aged less than 18 years have not been established. No data are available.

*Mode of administration*

Each tablet should be taken orally with or without food. Tablet should be swallowed whole.

**Contraindications**

- Hypersensitivity to the active substance or to any of the excipients listed in section "Composition".
- Pregnancy and breast-feeding (see section "Pregnancy, lactation").
- Concomitant use with simvastatin > 40 mg daily (see sections "Dosage/Administration", "Warnings and precautions", and "Interactions")

**Warnings and precautions**

Potential risk of myopathy with concomitant use of statins

Bempedoic acid increases plasma concentrations of statins (see section "Indications"). Patients receiving Nilemdo as adjunctive therapy to a statin should be monitored for adverse reactions that are associated with the use of high doses of statins. Statins occasionally cause myopathy. In rare cases, myopathy may take the form of rhabdomyolysis with or without acute renal failure secondary to myoglobinuria, and can lead to fatality. All patients receiving Nilemdo in addition to a statin should be advised of the potential increased risk of myopathy and told to report promptly any unexplained muscle pain, tenderness, or weakness. If such symptoms occur while a patient is receiving treatment with Nilemdo and a statin, a lower dose of the same statin or an alternative statin, or discontinuation of Nilemdo and initiation of an alternative lipid-lowering therapy should be considered under close monitoring of lipid levels and adverse reactions. If myopathy is confirmed by a creatine phosphokinase (CPK) level > 10× upper limit of normal (ULN), Nilemdo and any statin that the patient is taking concomitantly should be immediately discontinued.

Myositis with a CPK level > 10× ULN was rarely reported with bempedoic acid and background simvastatin 40 mg therapy. Doses of simvastatin > 40 mg should not be used with Nilemdo (see sections "Dosage/Administration" and "Contraindications").

Concomitant administration of Nilemdo with pravastatin doses more than 40 mg daily should be avoided (see section "Interactions").

*Increased serum uric acid*

Elevations in serum uric acid have occurred. Bempedoic acid may raise serum uric acid level due to inhibition of renal tubular OAT2 and may cause or exacerbate hyperuricaemia and precipitate gout in patients with a medical history of gout or predisposed to gout (see section "Undesirable effects"). Uric acid levels should be assessed periodically as clinically indicated. Patients should be monitored for

signs and symptoms of hyperuricemia and treated with urate-lowering drugs as appropriate. Treatment with Nilemdo should be discontinued if hyperuricaemia accompanied with symptoms of gout appear.

*Elevated liver enzymes*

In clinical trials, elevations of > 3× ULN in the liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) have been reported with bempedoic acid. These elevations have been asymptomatic and not associated with elevations ≥ 2× ULN in bilirubin or with cholestasis and have returned to baseline with continued treatment or after discontinuation of therapy. Liver function tests should be performed at initiation of therapy. Treatment with Nilemdo should be discontinued if an increase in transaminases of > 3× ULN persists (see section “Undesirable effects”).

*Hepatic impairment*

Patients with severe hepatic impairment (Child-Pugh C) have not been studied (see section “Pharmacokinetics”). Periodic liver function tests should be considered for patients with severe hepatic impairment.

*Renal impairment*

There is limited experience with Nilemdo in patients with severe renal impairment (defined as eGFR < 30 mL/min/1.73 $m^2$), and patients with ESRD requiring dialysis have not been studied (see section “Pharmacokinetics”). Additional monitoring for adverse reactions may be warranted in these patients when Nilemdo is administered.

*Excipients*

Nilemdo contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take this medicinal product.
This medicinal product contains less than 1 mmol sodium (23 mg) per 180 mg film-coated tablet (daily dose), that is to say essentially ‘sodium-free’.

**Interactions**

*Effect of Nilemdo on other medicinal products*

*Statins*
The pharmacokinetic interactions between bempedoic acid 180 mg and simvastatin 40 mg, atorvastatin 80 mg, pravastatin 80 mg, and rosuvastatin 40 mg were evaluated in clinical trials.

*Simvastatin*: Administration of a single dose of simvastatin 40 mg with steady-state bempedoic acid 180 mg resulted in a 2-fold increase in simvastatin acid exposure. When Nilemdo is coadministered with simvastatin, limit simvastatin dosage to 20 mg daily (or 40 mg daily for patients who can tolerate simvastatin 80 mg daily longterm without any signs of muscle toxicity) (see section “Warnings and

precautions"). Refer to the simvastatin product information for healthcare professionals for simvastatin dosing recommendations.

*Pravastatin:* Administration of pravastatin 80 mg with steady-state bempedoic acid 180 mg in healthy subjects resulted in 46% (1.5-fold) and 36%(1.4-fold) increases in pravastatin area under the curve (AUC) and maximum plasma concentration ($C_{max}$), respectively. Administration of pravastatin 40 mg with steady-state bempedoic acid 240 mg in healthy subjects resulted in 99% (2-fold) and 104% (2-fold) increases in pravastatin acid AUC and $C_{max}$, respectively. In the event of concomitant administration of Nilemdo and pravastatin, pravastatin doses more than 40 mg daily should be avoided.

*Atorvastatin and rosuvastatin*: Elevations of 1.4-fold to 1.5-fold in AUC of atorvastatin and rosuvastatin (administered as single doses) and/or their major metabolites were observed when coadministered with bempedoic acid 180 mg. Higher elevations have been observed when these statins were coadministered with a supratherapeutic 240 mg dose of bempedoic acid.

*Transporter-mediated drug interactions*

Bempedoic acid and its glucuronide weakly inhibit OATP1B1 and OATP1B3 at clinically relevant concentrations. Coadministration of bempedoic acid with medicinal products that are substrates of OATP1B1 or OATP1B3 (i.e., bosentan, fimasartan, asunaprevir, glecaprevir, grazoprevir, voxilaprevir, and statins such as atorvastatin, pravastatin, fluvastatin, pitavastatin, rosuvastatin, and simvastatin) may result in increased plasma concentrations of these medicinal products.

Bempedoic acid inhibits OAT2 *in vitro*, which may be the mechanism responsible for minor elevations in serum creatinine and uric acid (see section "Undesirable effects"). Inhibition of OAT2 by bempedoic acid may also potentially increase plasma concentrations of medicinal products that are substrates of OAT2. Bempedoic acid may also weakly inhibit OAT3 at clinically relevant concentrations.

*Ezetimibe*

Increases in AUC and $C_{max}$ for ezetimibe were less than 20% when a single dose of ezetimibe was taken with steady-state bempedoic acid. Total ezetimibe (ezetimibe and its glucuronide form) and ezetimibe glucuronide AUC and $C_{max}$ increased approximately 1.6- and 1.8-fold, respectively. This increase is likely due to inhibition of OATP1B1 by bempedoic acid, which results in decreased hepatic uptake and subsequently decreased elimination of ezetimibe-glucuronide. These elevations are not clinically meaningful and do not impact dosing recommendations.

*Warfarin*

*In vitro* studies indicate that bempedoic acid is not an inhibitor or inducer of CYP2C9. Because warfarin is primarily eliminated through CYP2C9, its pharmacokinetics is not expected to be altered by bempedoic acid; however, it is recommended to appropriately monitor international normalized ratio (INR) if bempedoic acid is coadministered with warfarin, another coumarin anticoagulant or fluindione.

*Other interactions*

Bempedoic acid had no effect on the pharmacokinetics or pharmacodynamics of metformin or the pharmacokinetics of oral contraceptive norethindrone/ethinyl estradiol (an active substance combination not authorised in Switzerland). The effect of bempedoic acid on other contraceptives has not been studied.

*Effect of other medicinal products on Nilemdo*

*Bile acid sequestrants (such as cholestyramine)*

The effects of bile acid sequestrants such as cholestyramine on bempedoic acid exposure has not been studied. It is anticipated that bile acid sequestrants may reduce bempedoic acid bioavailability. Concomitant administration with bempedoic acid is therefore not recommended.

*Transporter-mediated drug interactions*

*In vitro* drug interaction studies suggest bempedoic acid, as well as its active metabolite and glucuronide form, are not substrates of commonly characterized drug transporters with the exception of bempedoic acid glucuronide, which is an OAT3 substrate.

*Probenecid*

Probenecid, an inhibitor of glucuronide conjugation, was studied to evaluate the potential effect of these inhibitors on the pharmacokinetics of bempedoic acid. Administration of bempedoic acid 180 mg with steady-state probenecid resulted in a 1.7- and a 1.2-fold increase in bempedoic acid AUC and $C_{max}$, respectively. AUC and $C_{max}$ for bempedoic acid active metabolite (ESP15228) were increased 1.9- and 1.5-fold, respectively. These elevations are not clinically meaningful and do not impact dosing recommendations.

*Cytochrome P450 Substrates*

*In vitro* metabolic interaction studies suggest that bempedoic acid, as well as its active metabolite and glucuronide forms are not metabolised by and do not interact with cytochrome P450 enzymes.

**Pregnancy, lactation**

*Pregnancy*

Nilemdo is contraindicated during pregnancy (see section “Contraindications”).
There are no or limited amount of data from the use of Nilemdo in pregnant women. Studies in animals with bempedoic acid monotherapy have shown reproductive toxicity (see section “Preclinical data”).
Because bempedoic acid decreases cholesterol synthesis and possibly the synthesis of other cholesterol derivatives needed for normal foetal development, Nilemdo may cause foetal harm when

administered to pregnant women. Nilemdo should be discontinued prior to conception or as soon as pregnancy is recognized (see section “Contraindications”).

*Women of childbearing potential*

Women of childbearing potential should use effective contraception during treatment.

*Lactation*

It is unknown whether bempedoic acid/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded.
Because of the potential for serious adverse reactions, women taking Nilemdo should not breast-feed their infants. Nilemdo is contraindicated during breast-feeding.

*Fertility*

No data on the effect of Nilemdo on human fertility are available. Based on animal studies, no effect on reproduction or fertility is expected with Nilemdo (see section “Preclinical data”).

**Effects on ability to drive and use machines**

Nilemdo has no or negligible influence on the ability to drive and use machines.

**Undesirable effects**

*Summary of the safety profile*

The safety profile of Nilemdo has been studied in 4 placebo-controlled phase 3 primary hyperlipidaemia studies (N=3 621) including patients with hypercholesterolemia on maximum tolerated statin dose (2 studies; n=3 008) and patients whose maximally tolerated statin dose was the lowest approved dose or less (2 studies; n=613). The most commonly reported adverse reactions with Nilemdo during pivotal trials were hyperuricaemia (3.8%), pain in extremity (3.1%), anaemia (2.5%), and gout (1.4%). More patients on Nilemdo compared to placebo discontinued treatment due to muscle spasms (0.7% versus 0.3%), diarrhoea (0.5% versus <0.1%), pain in extremity (0.4% versus 0), and nausea (0.3% versus 0.2%), although differences between bempedoic acid and placebo were not significant. The safety profile in the cardiovascular outcomes study (N=13 965) was consistent with the overall safety profile described in the phase 3 primary hyperlipidaemia studies.

*Tabulated list of adverse reactions*

Adverse reactions reported with bempedoic acid, based on incidence rates from phase 3 primary hyperlipidaemia studies and exposure adjusted incidence rates from cardiovascular outcomes study, are displayed by system organ class and frequency below.
Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000) and very rare (< 1/10 000).

*Infections and infestations*

Common: upper respiratory tract infection, bronchitis

*Blood and lymphatic system disorders*

Common: anaemia

Uncommon: haemoglobin decreased

Rare: thrombocytosis, leukopenia

*Metabolism and nutrition disorders*

Common: gout, hyperuricaemia[a]

*Gastrointestinal disorders*

Common: abdominal pain or discomfort[b]

*Hepatobiliary disorders*

Common: aspartate aminotransferase increased

Uncommon: alanine aminotransferase increased, liver function test increased

*Musculoskeletal and connective tissue disorders*

Common: pain in extremity, back pain, muscle spasms, blood CPK increased

Uncommon: tendon rupture

*Renal and urinary disorders*

Common: glomerular filtration rate decreased,

Uncommon: blood creatinine increased, blood urea increased

a. Hyperuricaemia includes hyperuricaemia and blood uric acid increased
b. Abdominal pain or discomfort includes abdominal pain, abdominal pain upper, abdominal pain lower, and abdominal discomfort.

*Description of selected undesirable effects*

*Tendon rupture*

Nilemdo is associated with an increased risk of tendon rupture or injury. In clinical trials, tendon rupture occurred in 0.2% of patients treated with Nilemdo versus 0% of placebo-treated patients and involved the rotator cuff (the shoulder), biceps tendon, or Achilles tendon. Tendon rupture occurred within weeks to months of starting Nilemdo. Tendon rupture may occur more frequently in patients over 60 years of age, in those taking corticosteroid or fluoroquinolone drugs, in patients with renal failure, and in patients with previous tendon disorders.

Nilemdo should be discontinued immediately if the patient experiences rupture of a tendon. Discontinuing Nilemdo should be considered if the patient experiences joint pain, swelling, or inflammation. Patients should be advised to rest at the first sign of tendinitis or tendon rupture and to

contact their healthcare provider if tendinitis or tendon rupture symptoms occur. Alternative therapy should be considered in patients with a history of tendon disorders or tendon rupture.

*Hepatic enzyme elevations*

Increases in serum transaminases (AST and/or ALT) have been reported with Nilemdo. In the phase 3 primiary hyperlipidaemia studies, the incidence of elevations (≥ 3× ULN) in hepatic transaminase levels was 0.7% for patients treated with Nilemdo and 0.3% for placebo. In the cardiovascular outcomes study, the incidence of elevations ≥ 3× ULN in hepatic transaminase levels also occurred more frequently in bempedoic acid-treated patients (1.6%) than in placebo-treated patients (1.0%). These elevations in transaminases were generally asymptomatic, not associated with elevations ≥ 2× ULN in bilirubin or cholestasis, and returned to baseline with continued treatment or after discontinuation of therapy.

*Increased serum uric acid*

Increases in serum uric acid were observed in clinical trials with Nilemdo likely due to inhibition of renal tubular OAT2 (see section “Interactions”). In the phase 3 primary hyperlipidaemia studies, a mean increase of 47.6 micromole/L (0.8 mg/dL) in uric acid compared to baseline was observed with Nilemdo at week 12. The elevations in serum uric acid usually occurred within the first 4 weeks of treatment and returned to baseline following discontinuation of treatment. In the phase 3 primary hyperlipidaemia studies, gout was reported in 1.4% of patients treated with Nilemdo and 0.4% of patients treated with placebo (see section “Warnings and precautions”). In the cardiovascular outcomes study, a mean increase of 47.6 micromole/L (0.8 mg/dL) in uric acid compared to baseline was observed in bempedoic acid-treated patients at month 3, and gout was also reported more frequently in bempedoic acid-treated patients (3.1%) than placebo-treated patients (2.1%). In both treatment groups, patients who reported gout were more likely to have a medical history of gout and/or baseline levels of uric acid above the ULN.

*Effects on serum creatinine and blood urea nitrogen (BUN)*

Bempedoic acid has been shown to increase serum creatinine and BUN. In the phase 3 primary hyperlipidemia studies, a mean increase of 4.4 micromole/L (0.05 mg/dL) in serum creatinine and a mean increase of 0.61 mmol/L( 1.7 mg/dL) in BUN compared to baseline was observed with bempedoic acid at week 12. The elevations in serum creatinine and BUN usually occurred within the first 4 weeks of treatment, remained stable, and returned to baseline following discontinuation of treatment. Similar mean increases in serum creatinine (5.8 micromole/L (0.066 mg/dL)) and BUN (0.82 mmol/L (2.3 mg/dL)) were observed with bempedoic acid in the cardiovascular outcomes study. The observed elevations in serum creatinine may be associated with bempedoic acid inhibition of OAT2-dependent renal tubular secretion of creatinine (see section “Interactions”), representing a drug-endogenous substrate interaction, and does not appear to indicate worsening renal function. This effect should be considered when interpreting changes in estimated creatinine clearance in

patients on Nilemdo therapy, particularly in patients with medical conditions or receiving medicinal products that require monitoring of estimated creatinine clearance.

*Decreased haemoglobin*

Decreases in haemoglobin were observed in clinical trials with Nilemdo. In the phase 3 primary hyperlipidaemia studies, a decrease in haemoglobin from baseline of ≥ 2 g/dL and < lower limit of normal (LLN) was observed in 4.6% of patients in the Nilemdo group compared with 1.9% of patients on placebo. Greater than 5 g/dL and < LLN decreases in haemoglobin were reported at similar rates in Nilemdo and placebo groups (0.2% versus 0.2%, respectively). The decreases in haemoglobin usually occurred within the first 4 weeks of treatment and returned to baseline following discontinuation of treatment. Among patients who had normal haemoglobin values at baseline, 1.4% in the Nilemdo group and 0.4% in the placebo group experienced haemoglobin values below LLN while on treatment. In the phase 3 primary hyperlipidaemia studies, anaemia was reported in 2.5% of patients treated with Nilemdo and 1.6% of patients treated with placebo. In the cardiovascular outcomes study, similar decreases in haemoglobin were observed, and anaemia was also reported more frequently in bempedoic acid-treated patients (4.7%) compared to placebo-treated patients (3.9%).

*Increase in platelet count*

Approximately 9.5% of patients (versus 4.1% placebo) had increases in platelet counts of $100\times 10^9$/L or more on one or more occasion. Platelet count increase was asymptomatic, did not result in increased risk for thromboembolic events, and did not require medical intervention.

*Decrease in leucocytes*

Approximately 8.7% of Nilemdo-treated patients with normal baseline leucocyte count had a decrease to less than the lower limit of normal on one or more occasion (versus 6.2% placebo). Leucocyte decrease was generally asymptomatic and did not require medical intervention. In clinical trials, there was a small imbalance in skin or soft tissue infections, including cellulitis (0.7% versus 0.3%), but there was no imbalance in other infections.

*Increase in creatine kinase*

Approximately 1.0% of patients (versus 0.5% placebo) had elevations of CK levels of 5 or more times the normal value on one or more occasions, and 0.4% of patients (versus 0.2% placebo) had elevations of CK levels of 10 or more times.

*Elderly population*

Of the 3 621 patients treated in the bempedoic acid phase 3 primary hyperlipidaemia studies, 2 098 (58%) were > 65 years old. In the cardiovascular outcomes study, 4 141 patients (59%) treated with bempedoic acid were ≥65 years of age and 1 066 patients (15%) treated with bempedoic acid were ≥

75 years of age. No overall difference in safety was observed between elderly and the younger population.

*Reporting of suspected adverse reactions*

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the EIViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

**Overdose**

There is no clinical experience with Nilemdo overdose. Doses up to 240 mg/day (1.3 times the approved recommended dose) have been administered in clinical trials with no evidence of dose limiting toxicity.
No adverse effects were observed in animal studies at exposures up to 14-fold higher than those in patients treated with Nilemdo at 180 mg once daily.

*Treatment*

There is no specific treatment for a Nilemdo overdose. In the event of an overdose, the patient should be treated symptomatically, and supportive measures instituted as required.

**Properties/Effects**

*ATC code*

C10AX15

*Mechanism of action*

Bempedoic acid is an adenosine triphosphate citrate lyase (ACL) inhibitor that lowers low-density lipoprotein cholesterol (LDL-C) by inhibition of cholesterol synthesis in the liver. ACL is an enzyme upstream of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase in the cholesterol biosynthesis pathway. Bempedoic acid requires coenzyme A (CoA) activation by very long-chain acyl-CoA synthetase 1 (ACSVL1) to ETC-1002-CoA. ACSVL1 is expressed primarily in the liver and not in skeletal muscle. Inhibition of ACL by ETC-1002-CoA results in decreased cholesterol synthesis in the liver and lowers LDL-C in blood via upregulation of low-density lipoprotein receptors. Additionally, inhibition of ACL by ETC-1002-CoA results in concomitant suppression of hepatic fatty acid biosynthesis.

*Pharmacodynamics*

Administration of bempedoic acid alone and in combination with other lipid modifying medicinal products decreases LDL-C, non-high density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (apo B), total cholesterol (TC), and high-sensitivity C-reactive protein (hsCRP) in patients with hypercholesterolaemia.

Because patients with diabetes are at elevated risk for atherosclerotic cardiovascular disease, the clinical trials of Nilemdo included patients with diabetes mellitus. Among the subset of patients with diabetes, lower levels of HbA1c were observed as compared to placebo (on average 0.2%). In patients without diabetes, no difference in HbA1c was observed between Nilemdo and placebo and there were no differences in the rates of hypoglycaemia.

*Cardiac electrophysiology*

At a dose of 240 mg (1.3 times the approved recommended dose), bempedoic acid does not prolong the QT interval to any clinically relevant extent.

*Clinical efficacy*

*Clinical efficacy and safety in primary hypercholesterolaemia and mixed dyslipidaemia*
The efficacy of Nilemdo was investigated in four multi-centre, randomised, double-blind, placebo-controlled phase 3 primary hyperlipidaemia studies involving 3,623 adult patients with hypercholesterolaemia or mixed dyslipidaemia, with 2,425 patients randomised to bempedoic acid All patients received Nilemdo 180 mg or placebo orally once daily. In two trials, patients were taking background lipid-modifying therapies consisting of a maximum tolerated dose of statin, with or without other lipid-modifying therapies. Two trials were conducted in patients with documented statin intolerance. The primary efficacy endpoint in all Phase 3 trials was the mean percent reduction from baseline in LDL-C at week 12 as compared with placebo.
In both trials, the maximum LDL-C lowering effects were observed as early as week 4 and efficacy was maintained throughout the trials. These results were consistent across all subgroups studied in both trials, including age, gender, race, ethnicity, region, history of diabetes, baseline LDL-C, body mass index (BMI), HeFH status, and background therapies.

*Combination therapy with statins*

Study 1002-047 was a multi-centre, randomised, double-blind, placebo-controlled, 52-week phase 3 primary hyperlipidaemia study in patients with atherosclerotic cardiovascular disease (ASCVD) and/or heterozygous familial hypercholesterolaemia (HeFH). Efficacy of Nilemdo was evaluated at week 12. The trial included 779 patients randomised 2:1 to receive either Nilemdo (n=522) or placebo (n=257) as add-on to a maximum tolerated lipid lowering therapy. Maximum tolerated lipid lowering therapy was defined as a maximum tolerated statin dose (including statin regimens other than daily dosing and no to very low doses) alone or in combination with other lipid-lowering therapies. Patients on simvastatin 40 mg/day or higher were excluded from the trial.
Overall, the mean age at baseline was 64 years (range: 28 to 91 years), 51% were ≥ 65 years old, 36% were women, 94% were White, 5% were Black, and 1% were Asian. The mean baseline LDL-C was 3.1 mmol/L (120.4 mg/dL) and the median baseline hsCRP was 1.7 mg/L. At the time of randomisation, 91% of patients were receiving statin therapy and 53% were receiving high-intensity

statin therapy. The difference between Nilemdo and placebo in mean percent change in LDL-C from baseline to Week 12 was -17% (95% CI: -21%, -14%; p < 0.001).
Study 1002-040 was a multi-centre, randomised, double-blind, placebo-controlled 52-week phase 3 primary hyperlipidaemia study evaluating safety and efficacy of bempedoic acid in patients with ASCVD and/or HeFH. Efficacy of Nilemdo was evaluated at week 12. The trial included 2 230 patients randomised 2:1 to receive either Nilemdo (n=1 488) or placebo (n=742) as add-on to a maximum tolerated lipid lowering therapy. Maximum tolerated lipid lowering therapy was defined as a maximum tolerated statin dose (including statin regimens other than daily dosing and very low doses) alone or in combination with other lipid lowering therapies. Patients on simvastatin 40 mg per day or higher and patients on PCSK9 inhibitors were excluded from the trial.
Overall, the mean age at baseline was 66 years (range: 24 to 88 years), 61% were ≥ 65 years old, 27% were women, 96% were White, 3% were Black, and 1% were Asian. The mean baseline LDL-C was 2.7 mmol/L (103.2 mg/dL) and the median baseline hsCRP was 1.5 mg/L. At the time of randomisation, all patients were receiving statin therapy and 50% were receiving high-intensity statin therapy. The difference between Nilemdo and placebo in mean percent change in LDL-C from baseline to Week 12 was -18% (95% CI: -20%, -16%; p < 0.001). A significantly higher proportion of patients achieved an LDL-C of < 1.81 mmol/L (< 70 mg/dL) in the Nilemdo group as compared with placebo at week 12 (32% versus 9%, P < 0.001).

*Statin intolerant patients*

Study 1002-048 was a multi-centre, randomised, double-blind, placebo-controlled 12-week phase 3 primary hyperlipidaemia study evaluating the efficacy of Nilemdo versus placebo in lowering LDL-C when added to ezetimibe in patients with elevated LDL-C who had a history of statin intolerance and were unable to tolerate more than the lowest approved starting dose of a statin. The trial investigated 269 patients randomised 2:1 to receive either bempedoic acid (n=181) or placebo (n=88) as add-on to ezetimibe 10 mg daily for 12 weeks.
Overall, the mean age at baseline was 64 years (range: 30 to 86 years), 55% were ≥ 65 years old, 61% were women, 89% were White, 8% were Black, 2% were Asian, and 1% were other. The mean baseline LDL-C was 3.3 mmol/L (127.6 mg/dL). At the time of randomisation, 33% of patients on bempedoic acid versus 28% on placebo were receiving statin therapy at less than or equal to lowest approved doses. Bempedoic acid significantly reduced LDL-C from baseline to week 12 compared with placebo (p < 0.001). Bempedoic acid also significantly reduced non-HDL-C, apo B, and TC.
Study 1002-046 was a multi-centre, randomised, double-blind, placebo-controlled 24-week phase 3 primary hyperlipidaemia study evaluating the efficacy of Nilemdo versus placebo in patients with elevated LDL-C who were statin-intolerant or unable to tolerate two or more statins, one at the lowest dose. Patients able to tolerate a dose that was less than the approved starting dose of a statin were allowed to stay on that dose during the study. Efficacy of bempedoic acid was evaluated at week 12. The trial included 345 patients randomised 2:1 to receive either bempedoic acid (n=234) or placebo

(n=111) for 24 weeks. At the time of randomisation, 8% of patients on bempedoic acid versus 10% on placebo were receiving statin therapy at less than the lowest approved doses and 36% of patients on bempedoic acid versus 30% of patients on placebo were on other nonstatin lipid-modifying therapies. Overall, the mean age at baseline was 65 years (range: 26 to 88 years), 58% were ≥ 65 years old, 56% were women, 89% were White, 8% were Black, 2% were Asian, and 1% were other. The mean baseline LDL-C was 4.1 mmol/L (157.6 mg/dL).
Bempedoic acid significantly reduced LDL-C from baseline to week 12 compared with placebo ($p < 0.001$). Bempedoic acid also significantly reduced non-HDL-C, apo B, and TC.

*Treatment in the absence of lipid-modifying therapies*

In Study 1002-046, 133 patients in the bempedoic acid group and 67 patients in the placebo group were on no background lipid-modifying therapies. Bempedoic acid significantly reduced LDL-C from baseline to week 12 compared with placebo in this subgroup. The difference between bempedoic acid and placebo in mean percent change in LDL-C from baseline to week 12 was -22.1% (CI: -26.8%, -17.4%; $p < 0.001$).
In all four trials, the maximum LDL-C lowering effects were observed as early as week 4 and efficacy was maintained throughout the trials. These results were consistent across all subgroups studied in any of the trials, including age, gender, race, ethnicity, region, history of diabetes, baseline LDL-C, body mass index (BMI), HeFH status, and background therapies.

*Clinical efficacy and safety in prevention of cardiovascular events*

Study 1002-043 was a multi-centre randomised, double-blind, placebo-controlled, event-driven trial in 13 970 adult patients with established atherosclerotic cardiovascular disease (CVD) (70%), or at high risk for atherosclerotic CVD (30%). Patients with established CVD had documented history of coronary artery disease, symptomatic peripheral arterial disease, and/or cerebrovascular atherosclerotic disease. Patients without established CVD were considered at high risk for CVD based on meeting at least one of the following criteria: (1) diabetes mellitus (type 1 or type 2) in women over 65 years of age, or men over 60 years of age, or (2) a Reynolds Risk score >30% or a SCORE Risk score >7.5% over 10 years, or 3) a coronary artery calcium score >400 Agatston units at any time in the past. Patients were randomised 1:1 to receive either Nilemdo 180 mg per day (n = 6 992) or placebo (n = 6 978) alone or as an add on to other background lipid lowering therapies that could include very low doses of statins. Overall, more than 95% of patients were followed until the end of the trial or death, and less than 1% were lost to follow up. The median follow-up duration was 3.4 years.
At baseline, the mean age was 65.5 years, 48% were women, 91% were white. Selected additional baseline characteristics included hypertension (85%), diabetes mellitus (46%), pre-diabetes mellitus (42%), current tobacco user (22%), eGFR < 60 mL/min per 1.73 $m^2$ (21%), and a mean body mass index 29.9 $kg/m^2$. The mean baseline LDL-C was 3.6 mmol/L (139 mg/dL). At baseline, 41% of

patients were taking at least one lipid modifying therapy including ezetimibe (12%), and very low dose of statins (23%).
Nilemdo significantly reduced the risk for the primary composite endpoint of major adverse cardiovascular events (MACE-4) consisting of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, or coronary revascularization by 13% compared to placebo (HR: 0.87; 95% CI: 0.79, 0.96; p = 0.0037); and the risk of the key secondary MACE-3 composite endpoint (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) was significantly reduced by 15% compared to placebo (HR: 0.85; 95% CI: 0.76, 0.96; p = 0.0058). The primary composite endpoint result was generally consistent across prespecified subgroups (including baseline age, race, ethnicity, sex, LDL-C category, statin use, ezetimibe use, and diabetes). Impact of Nilemdo on the individual components of the primary endpoint included a 27% reduction in the risk of non-fatal myocardial infarction and a 19% reduction in the risk of coronary revascularization compared to placebo. There was no statistically significant difference in the reduction of non-fatal stroke and risk of cardiovascular death compared to placebo.
Further, the difference between Nilemdo and placebo in mean percent change in LDL-C from baseline to month 6 was -20% (95% CI: -21%, -19%).

*Safety and efficacy in paediatric patients*

Swissmedic has deferred the obligation to submit the results of studies with Nilemdo in paediatric population from 4 to less than 18 years of age in the treatment of elevated cholesterol. See section “Dosage/administration” for information on paediatric use.

**Pharmacokinetics**

*Absorption*

Pharmacokinetic data indicate that bempedoic acid is absorbed with a median time to maximum plasma concentrations ($C_{max}$) of 3.5 hours when administered orally as Nilemdo 180 mg tablets. Bempedoic acid pharmacokinetic parameters are presented as the mean [standard deviation (SD)] unless otherwise specified. Bempedoic acid is a prodrug that is activated intracellularly by ACSVL1 to ETC-1002-CoA. The bempedoic acid steady-state $C_{max}$ and AUC following multiple-dose administration in patients with hypercholesterolaemia were 24.8 (6.9) microgram/mL and 348 (120) microgram·h/mL, respectively.. Bempedoic acid steady-state pharmacokinetics were generally linear over a range of 120 mg to 220 mg. There were no time-dependent changes in bempedoic acid pharmacokinetics following repeat administration at the recommended dosage, and bempedoic acid steady-state was achieved after 7 days. The mean accumulation ratio of bempedoic acid was approximately 2.3-fold.
Concomitant food administration had no effect on the oral bioavailability of bempedoic acid when administered as Nilemdo 180 mg tablets.

*Distribution*

The bempedoic acid apparent volume of distribution (V/F) was 18 L. Plasma protein binding of bempedoic acid, its glucuronide and its active metabolite, ESP15228, were 99.3%, 98.8% and 99.2%, respectively. Bempedoic acid does not partition into red blood cells.

*Metabolism*

The primary route of elimination for bempedoic acid is through metabolism to the acyl glucuronide. Bempedoic acid is also reversibly converted to an active metabolite (ESP15228) based on aldo-keto reductase activity. Mean plasma AUC metabolite/parent drug ratio for ESP15228 following repeat-dose administration was 18% and remained constant over time. Both bempedoic acid and ESP15228 are converted to inactive glucuronide conjugates *in vitro* by UGT2B7. Bempedoic acid, ESP15228 and their respective conjugated forms were detected in plasma with bempedoic acid accounting for the majority (46%) of the $AUC_{0\text{-}48h}$ and its glucuronide being the next most prevalent (30%). ESP15228 and its glucuronide represented 10% and 11% of the plasma $AUC_{0\text{-}48h}$, respectively.
The steady-state $C_{max}$ and AUC of the equipotent active metabolite (ESP15228) of bempedoic acid in patients with hypercholesterolaemia were 3.0 (1.4) microgram/mL and 54.1 (26.4) microgram·h/mL, respectively. ESP15228 likely made a minor contribution to the overall clinical activity of bempedoic acid based on systemic exposure and pharmacokinetic properties.

*Elimination*

The steady-state clearance (CL/F) of bempedoic acid determined from a population PK analysis in patients with hypercholesterolaemia was 12.1 mL/min after once-daily dosing; renal clearance of unchanged bempedoic acid represented less than 2% of total clearance. The mean (SD) half-life for bempedoic acid in humans was 19 (10) hours at steady-state.
Following single oral administration of 240 mg of bempedoic acid (1.3 times the approved recommended dose), 62.1% of the dose (bempedoic acid and its metabolites) was recovered in urine, primarily as the acyl glucuronide conjugate of bempedoic acid, and 25.4% was recovered in faeces. Less than 5% of the administered dose was excreted as unchanged bempedoic acid in faeces and urine combined.
*Kinetics in specific patient groups*

*Hepatic impairment*

The pharmacokinetics of bempedoic acid and its metabolite (ESP15228) was studied in patients with normal hepatic function or mild or moderate hepatic impairment (Child-Pugh A or B) following a single dose (n=8/group). Compared to patients with normal hepatic function, the bempedoic acid mean $C_{max}$ and AUC were decreased by 11% and 22%, respectively, in patients with mild hepatic impairment and by 14% and 16%, respectively, in patients with moderate hepatic impairment. This is not expected to result in lower efficacy.

Bempedoic acid was not studied in patients with severe hepatic impairment (Child-Pugh C).

*Renal impairment*

Pharmacokinetics of bempedoic acid was evaluated in a population PK analysis performed on pooled data from all clinical trials (n=2,261) to assess renal function on the steady-state AUC of bempedoic acid and in a single-dose pharmacokinetic study in subjects with varying degrees of renal function. Compared to patients with normal renal function, the mean bempedoic acid exposures were higher in patients with mild or moderate renal impairment by 1.4-fold (90% PI: 1.3, 1.4) and 1.9-fold (90% PI: 1.7, 2.0), respectively (see section “Warnings and Precautions”).
There is limited information in patients with severe renal impairment; in a single dose study, the bempedoic acid AUC was increased by 2.4-fold in patients (n=5) with severe renal impairment (eGFR < 30 mL/min/1.73 $m^2$) compared to those with normal renal function. Clinical studies of Nilemdo did not include patients with ESRD on dialysis (see section “Warnings and Precautions”).

*Age, weight, gender and race*

The pharmacokinetics of bempedoic acid were not affected by age, gender, or race. Body weight was a statistically significant covariate. The lowest quartile of body weight (< 73 kg) was associated with an approximate 30% greater exposure. The increase in exposure was not clinically significant and no dose adjustments are recommended based on weight.

**Preclinical data**

*Repeat dose toxicity*

Deaths occurred in repeat-dose studies within the first 2 weeks of treatment in rats at exposures ≥ 9 times and in monkeys at exposures ≥ 15 times the systemic exposure in humans at 180 mg. Severely reduced blood glucose occurred within hours of dosing and preceded toxic effects at high doses leading to moribundity when untreated. Increased liver weight and hepatocellular hypertrophy were observed in rats and were partially reversed after the 1-month recovery at ≥ 30 mg/kg/day or 4 times the exposure in humans at 180 mg. Reversible, nonadverse changes in laboratory parameters indicative of these hepatic effects, and decreases in red blood cell, urea nitrogen, creatinine and coagulation parameters were observed in animals at doses lower than those associated with mortality. The NOAEL for adverse response in the chronic studies was 10 mg/kg/day and 60 mg/kg/day associated with exposures below and 15 times the human exposure at 180 mg in rats and monkeys, respectively.

*Mutagenicity*

The standard battery of genotoxicity studies has not identified any mutagenic or clastogenic potential of bempedoic acid.

*Carcinogenicity*

In full lifetime carcinogenicity studies in rodents, bempedoic acid increased the incidence of hepatocellular and thyroid gland follicular tumours in male rats and hepatocellular tumours in male mice. Because these are common tumours observed in rodent lifetime bioassays and the mechanism for tumourigenesis is secondary to a rodent-specific PPAR alpha activation, these tumours are not considered to translate to human risk.

*Reproductive toxicity*

Bempedoic acid was not teratogenic or toxic to embryos or foetuses in pregnant rabbits at doses up to 80 mg/kg/day or 12 times the systemic exposure in humans at 180 mg. Pregnant rats given bempedoic acid at 10, 30, and 60 mg/kg/day during organogenesis had decreased numbers of viable foetuses and reduced foetal body weight at ≥ 30 mg/kg/day or 4 times the systemic exposure in humans at 180 mg. An increased incidence of foetal skeletal findings (bent scapula and ribs) were observed at all doses, at exposures below the systemic exposure in humans at 180 mg. In a pre- and post-natal development study, pregnant rats administered bempedoic acid at 5, 10, 20 and 30 mg/kg/day throughout pregnancy and lactation had adverse maternal effects at ≥ 20 mg/kg/day and reductions in numbers of live pups and pup survival, pup growth and learning and memory at ≥ 10 mg/kg/day, with maternal exposures at 10 mg/kg/day, less than the exposure in humans at 180 mg.
Administration of bempedoic acid to male and female rats prior to mating and through gestation day 7 in females resulted in changes in estrous cyclicity, decreased numbers of corpora lutea and implants at ≥ 30 mg/kg/day with no effects on male or female fertility or sperm parameters at 60 mg/kg/day (4 and 9 times the systemic exposure in humans at 180 mg, respectively).

**Other information**

*Incompatibilities*

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

*Shelf life*

Do not use this medicine after the expiry date ("EXP") stated on the pack.

*Special precautions for storage*

Do not store above 30°C. Keep out of the reach of children.

**Authorisation number**

67583 (Swissmedic)

**Packs**

Packs with 28 and 98 film-coated tablets. [B]

**Marketing authorisation holder**

Daiichi Sankyo (Schweiz) AG, Zurich

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